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| 09/652,376 | 08/31/2000 | Arun Kumar Sinha | U 012930 | 4436 |
| 140 | 7590 | 01/25/2006 | EXAMINER | |
| LADAS & PARRY 26 WEST 61ST STREET NEW YORK, NY 10023 | | | KEYS, ROSALYND ANN | |
| | | | ART UNIT | PAPER NUMBER |
| | | | 1621 | |
| DATE MAILED: 01/25/2006 | | | | |

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/652,376

Applicant(s)

SINHA, ARUN KUMAR

Examiner

Rosalynd Keys

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 November 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1, 2 and 4-7 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 2 and 4-7 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

1. Claims 1, 2 and 4-7 are pending.
Claims 1, 2 and 4-7 are rejected.
Claims 3 and 8-12 are cancelled.

Continued Examination Under 37 CFR 1.114

2. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on November 21, 2005 has been entered.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.
4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1, 2 and 4-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Devgan et al. (Aust. J. Chem., 1968, 21, 3001-3003) alone or in view of Patra et al. (Journal of Natural Products, Vol. 44, No. 6, November-December 1981, pages 668 and 669) and further in view of March (Advanced

Organic Chemistry: Reactions, Mechanisms, and Structure, third edition, 1985, pp. 691-700 and 1093-1096) and Ma (US 3,757,490).

The instant claims are directed to a process for preparing 1-Propyl-2,4,5-trimethoxybenzene of the formula I from crude calamus oil from a tetraploid or hexaploid *Acorus calamus* wherein said crude calamus oil contains alpha, beta and gamma asarone comprising a) mixing crude calamus oil and a solvent selected from the group consisting of ethanol, methanol, THF, DCM, toluene and chloroform to prepare a solution; b) hydrogenation of the solution in the presence of a catalyst at a pressure of 10-40 psi and a temperature in the range of 15-40°C; c) filtering the catalyst and removing the solvent under reduced pressure in the range of 10-100 mm Hg; and d) separating the 1-propyl-2,4,5-trimethoxybenzene of the formula I from the calamus oil on a silica gel column by using an eluent to obtain 1-propyl-2,4,5-trimethoxybenzene of the formula I in liquid form with 85-97% purity. The toxicity of the hydrogenated calamus oil can be two times less than the starting calamus oil (see claim 4). The reduced calamus oil can have a novel honey and roses aroma (see claim 5). The 1-Propyl-2,4,5-trimethoxybenzene obtained can have a novel sweet ylang, slightly spicy and fruity aroma (see claim 6). The calamus oil can be extracted from specific asarone rich plants (see claim 7).

Devgan et al. teach a) a solution of gamma-asarone in alcohol; b) hydrogenating the solution in the presence of palladium-charcoal; c) filtering the catalyst off and removing the alcohol under suction; and the residue was chromatographed over neutral alumina and eluted with petroleum to give dihydro-gamma-asarone, which corresponds to the compound having the formula I in claim 1 (see page 3003 under the title Dihydro-gamma-asarone (II)).

The instant claims differ from Devgan et al. in that the instant invention employs crude calamus oil containing alpha, beta and gamma asarone as the starting material, whereas Devgan et al. employs gamma-asarone. However, alpha, beta and gamma-asarone are isomers of one another, differing only in the position of the double bond in the side chain. One having ordinary skill in the art at the time the

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invention was made would have found it obvious to utilize the process of Devgan et al. to obtain the dihydro derivatives of alpha, beta and gamma-asarones, since alpha, beta and gamma-asarone are of such close structural similarity that they would be expected to react similarly. This is further evidenced by the teachings of Patra et al., which shows that catalytic hydrogenation of beta-asarone in the presence of 10% Pd/C in ethanol also gives the dihydroderivative of formula I (see entire disclosure in particular the paragraph above the acknowledgements on page 669). A long line of cases have held that the mere use of a different starting material, whether novel or known, in a conventional process to produce the product one would expect therefrom does not render the process unobvious. See for example *In re Surrey et al.* (CCPA 1963) 319 F2d 233, 138 USPQ 67; *In re Larsen* (CCPA 1961) 292 F2d 531, 130 USPQ 209; and *In re Durden, Jr. et al.* (CAFC 1985) 763 F2d 1406, 226 USPQ 359. The skilled artisan would have been further motivated to utilize the process of Devgan et al. because it allows the skilled artisan to isolate dihydro asarones, which are known to be useful for making antipsychotic agents.

The instant claims further differ from Devgan et al. in that Devgan fail to disclose a specific hydrogenation temperature and pressure, instead Devgan et al. teach that the hydrogenation practically stopped at 24°/706 mm).

March teaches that almost all known alkenes add hydrogen at temperatures between 0 and 275°C (see page 692). March teaches that many functional groups may be present in the molecule, e.g., OH, COOH, NH₂, CHO, COR, COOR, OR CN; and that although, some of these groups are also susceptible to catalytic hydrogenation, it is usually possible to find conditions under which double bonds can be reduced selectively (see page 692 and pages 1093-1096). Alpha, beta- and gamma-asarone each contain the functional group COR. March teaches that hydrogenations in most cases are carried out at room temperature and just above atmospheric pressure, but some double bonds are more resistant and require higher temperatures and pressures (see page 693). March teaches that catalytic hydrogenation is the method most often used to reduce double bonds and that palladium-on-carbon is one of the most

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effective catalysts utilized (see pages 692 and 693). Both Devgan et al. and the applicants utilize Pd/C as a catalyst for conducting their hydrogenation processes. One having ordinary skill in the art at the time the invention was made would have found it obvious to utilize the conventional hydrogenation temperatures and pressures, as taught by March, to hydrogenate alpha, beta and gamma-asarone to obtain the dihydro derivative, especially since a temperature and pressure within this range has already been shown to be effective for reducing gamma-asarone.

Devgan et al. fail to disclose the toxicity and aroma of the obtained hydrogenated asarone. However, one having ordinary skill in the art would expect the hydrogenated asarone of Devgan et al. to have the claimed characteristics since, a compound and its properties are inseparable. In re Papesch, 315 F.2d 381, 137 USPQ 43 (CCPA 1963).

Devgan et al. fail to disclose the concentration of catalyst utilized. However, changes in temperature, concentrations, or other process conditions of an old process does not impart patentability unless the recited ranges are critical, i.e., they produce a new and unexpected result. In re Aller et al., (CCPA 1955) 220 F.2d 454, 105 USPQ 233.

Devgan et al. fail to disclose the purity of the obtained dihydro asarone. However, when claiming a purer form of a known compound, it must be demonstrated that the purified material possesses properties and utilities not possessed by the unpurified material. Ex parte Reed, 135 U.S.P.Q. 34, 36 (P.O.B.A. 1961), on reconsideration, Ex parte Reed, 135 U.S.P.Q. 105 (P.O.B.A. 1961).

Devgan et al. utilize a different adsorbent in step d). However, one having ordinary skill in the art would have found it obvious to utilize any adsorbent known for its use in chromatography in order to identify the product obtained (see column 3, lines 5-8 of the Ma patent, which teaches that alumina and silica gel are common adsorbents used in liquid-liquid and solid-liquid chromatography).

Devgan et al. further differ from the instant invention in the origin of the asarones. However, the origin of the asarones appears to be irrelevant, since the structure of the asarones is the same regardless of

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its origin. See Devgan et al. wherein a gamma-asarone obtained from *Caesulla Axillaries* oil undergoes the same hydrogenation, i.e., mixing the asarone with an alcohol and hydrogenating the mixture in the presence of Pd/C, and produces the same product, i.e., the dihydro derivative, as the beta-asarone obtained from *Acorus Calamus* as taught by Patra et al.

Response to Arguments

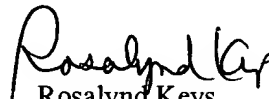
5. Applicant's arguments filed August 19, 2005 have been fully considered but they are not persuasive. The Examiner believes that whether one hydrogenates alpha-asarone alone, gamma-asarone alone, as taught by Devgan et al., or beta-asarone alone, as taught by Patra et al, or in combination as claimed, the result would be the same obtainment of the dihydro derivative. The Examiner believes that there is nothing in the calamus oil that would hinder each of the asarones present therein from undergoing hydrogenation in the manner taught by Devgan et al. When applying the process of the Devgan et al. to the instant calamus oil the skilled artisan may need to adjust the hydrogenation conditions, i.e. the amount of hydrogenating substance or the time of hydrogenation, to account for the additional asarones present in the starting material. However, any such adjustments would be obvious and are within the level of ordinary skill in the art. The Examiner believes that a prima facie case of obviousness exists because regardless of whether there is one asarone or a mixture of asarones in the starting material the skilled artisan is taught by Devgan et al. that one can obtain the dihydro-derivative of an asarone by conducting certain steps. The ability to hydrogenate beta and gamma asarone to obtain the dihydro derivative is taught in the prior art (see Devgan et al. and Patra et al.). Also the steps utilized by the Applicants to obtain the dihydro derivative, i.e., 1-propyl-2,4,5-trimethoxybenzene, are essentially the same as those taught by Devgan et al. other than the difference pointed out in the above rejection. Thus, when viewed as a whole the Examiner believes that the prior art teaches or at least fairly suggests the instant claimed invention.

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6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rosalynd Keys whose telephone number is 571-272-0639. The examiner can normally be reached on M and F 3:00-8:00 pm and T-TR 5:30-10:30 am.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


Rosalynd Keys
Primary Examiner
Art Unit 1621

January 20, 2006